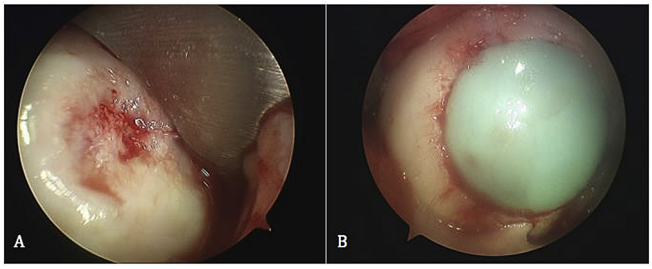

Figure 1. (A) Outerbridge Grade IV osteochondral defect of medial femoral condyle. (B) 15×11 mm Chondrofix Osteochonfral Allograft immediately after implantation

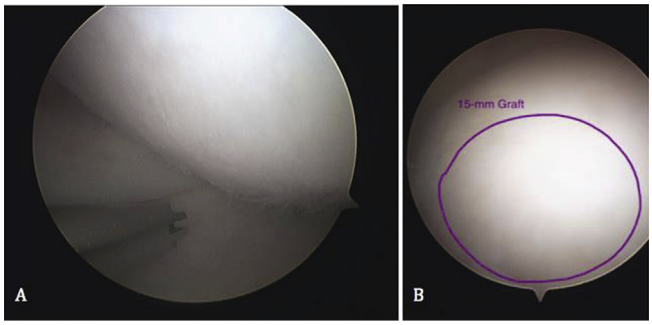

Figure 3. Arthroscopic examination of intact Chondrofix® Osteochondral Allograft 25 months after implantation revealing smooth borders without step-off (A,B).

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DIFFERENCES IN CARTILAGE REPAIR OF LOADING AND UNLOADING ENVIRONMENT IN THE RAT KNEE

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Purpose: We investigated histopathologically and immunohistochemically effects of loading on cartilage repair in rat full-thickness articular cartilage defects.
Methods: A total of 40 male 9-week-old Wistar rats were used. Full-thickness articular cartilage defects were created over the capsule at the loading portion in the medial condyle of the femur. Twenty rats were randomly allocated into each of a loading group and non-loading group. Twenty rats from these two groups were later randomly allocated to each of 2 groups for evaluation at 1 and 2 weeks after surgery. At the end of each period, the tissue of the defects were examined histopathologically and immunohistochemically.
Results: In both groups at 1 and 2 weeks, the defects were filled with mixture of granulation tissue and some remnants of hyaline cartilage. The repair tissue were not stained with Toluidine blue in the both groups. However, the adjacent articular cartilage to repair tissue in a loading group were more strongly and thickly stained with Toluidine blue than that in non-loading group. Strong staining of type I collagen was observed in repair tissue of the both groups. The area stained with type I collagen in non-loading group was smaller than that in loading groups. However, apparent staining of type II collagen was not detected in any repair tissue of the both groups.
Conclusions: Non-weight bearing in the early phase of an articular cartilage defect may be accompanied by a good tissue repair, althogh non-weight bearing may decrease the function of adjacent normal cartilage.

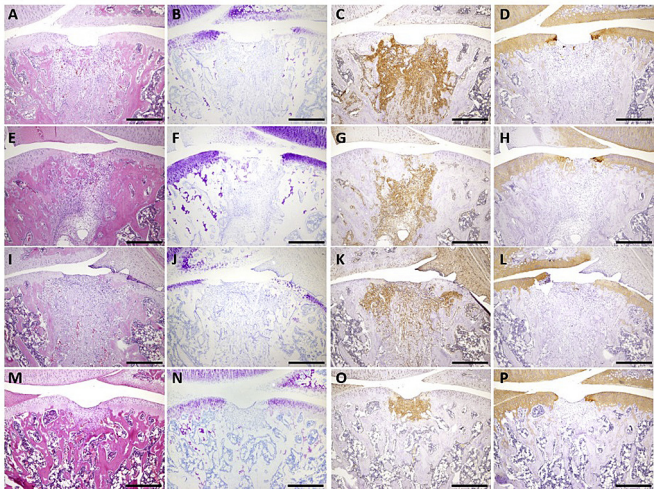

Fig. 1. Histopathological and immunohistochemical staining of the repair tissue.Sagittal sections of full-thickness articular cartilage defects in the loading group (A-D, I-L) and non-loading group (E-H, M-P) at 1 week (A-D, E-H) and 2 weeks (I-L, M-P). The sections were stained with hematoxylin and eosin (A, E, I, M), Toluidine Blue (B, F, J, N) and immunohistochemical staining for type I collagen (C, G, K, O) and type II collagen (D, H, L, P). Scale bar = 500 μm.

Cell Signaling

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DKK1, FRZB, GREM1 PREVENT IL1B INDUCED ARTICULAR CARTILAGE DEGRADATION

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Purpose: Osteoarthritis (OA) is a multifactorial disease characterized by progressive degradation of articular cartilage leading to loss of joint function. It affects several million people in the world. Currently there is no cure for OA. In a subset of patients OA is associated with hypertrophic differentiation of articular chondrocytes. This process normally occurs in the growth plate. Healthy articular cartilage is protected against hypertrophy. Our group identified DKK1, FRZB (WNT antagonists) and GREM1 (BMP antagonist) as the natural brakes on hypertrophic differentiation and regulation of the maintenance of the articular phenotype. Moreover, we previously demonstrated that decreased production of DKK1, FRZB, GREM1 in human chondrocytes has been associated with cartilage hypertrophy in OA. In this project, we hypothesize that DKK1, FRZB, GREM1 are the gatekeepers for the maintenance of homeostasis in articular cartilage. To prove this, we investigated whether knockdown of DKK1, FRZB and GREM1 is sufficient to cause hypertrophic differentiation in healthy articular chondrocytes. Furthermore, we investigated the influence of catabolic factors such as interleukin-1β (IL-1β) on the gene transcription levels of DKK1, FRZB, GREM1. We found that the presence of DKK1, FRZB and GREM1 is sufficient to inhibit the catabolic effects of IL-1β.
Methods: Human primary chondrocytes (hCh) were isolated from cartilage as described previously by our group. We isolated a neutralizing VhH antibody against DKK1 from a llama VhH library and used this to block DKK1 activity in human primary chondrocytes cultured in monolayer. The chondrocytes were cultured in chondrocyte proliferation medium containing 5 μg/ml neutralizing antibody for 1 week. Normal IgG served as a negative control. The neutralizing function of the antibody was tested before use. Isolated chondrocytes were exposed to 10ng/ml of recombinant human IL-1β, and 200ng/ml of each of DKK1, FRZB, GREM1 (all recombinant proteins are from R&D systems). Cells received no medium refreshment after stimulation and were cultured up to 48 hours.
Results: In the presence of recombinant DKK1 protein the mRNA expression of the WNT target gene AXIN2 was downregulated. In presence of both DKK1 and the DKK1 neutralizing antibody, AXIN2 mRNA was upregulated suggesting that the WNT signal pathway activity was (re) activated. MMP1, 3 and 13 as well as RUNX2 were upregulated in cells with DKK1 knockdown. The expression of Col10 could not be detected. This